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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/870,358	05/30/2001	Chong Jin Oon	20781-703	8357

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EXAMINER	
GOLDBERG, JEANINE ANNE	

ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/870,358	OON ET AL.	
	Examiner	Art Unit	
	Jeanine A Goldberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,4-6,13-22,24-33 and 35* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,4-6,13-22,24-33 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This action is in response to the papers filed November 26, 2003 and December 22, 2003. Currently, Claims 1, 4-6, 13-22, 24-33, 35 are pending.

2. This action contains new grounds of rejection.

3. Any objection or rejection not reiterated herein, has been withdrawn in view of the amendments to the claims and applicants remarks.

Election/Restrictions

Restriction Requirement:

4. In view of the amendments to the claims to require SEQ ID NO: 1 and 2, the restriction requirement has been withdrawn. In the event that the claims are further amended such that SEQ ID NO: 1 and 2 are no longer required in the independent claim, the restriction requirement for detecting various mutations may be re-instated.

Priority

5. This application claims priority to foreign application Singapore 20004041-0, filed July 18, 2000. A certified copy of the application has been provided.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 32-33, 35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are broadly drawn to a method for evaluating whether a sample contains HBV that may be resistant to anti-HBV drug treatment by detecting a mutation at position 130 where the identification of said mutation is indicative of the sample containing HBV that may be resistant to anti-HBV drug treatment.

The specification teaches the detecting and identification of HBV surface antigen mutants in Singapore adults and vaccinated infants with high anti-HBs levels but negative for surface antigen (Example 1, page 31). The results of the mutation analysis state that "there are also three cases here with the G130 D mutation (Table 2) that is recently found in one case report to be associated with lamivudine therapy (page 31, col. 30-32).

The art teaches the presence of G130D mutations in isolates of HBV.

Neither the art nor the specification teaches how to use the invention as broadly as claimed. The art does not teach any association of G130D with any resistance to anti-HBV drug treatment. Moreover, there is no indication in the specification that G130D mutation is associated with anti-HBV drug treatment resistance. The specification reports three cases with the G130D mutation that is recently found in one case report to be associated with lamivudine therapy. There is no indication whether

this finding is present in a representative sample, whether the mutation is associated with resistance to lamivudine therapy, for example. The detection of the mutation in three cases, without information about the presence in normal individuals also requires further experimentation. The teachings of the specification do not establish that one could actually detect the presence of a mutation at position 130 as indicative that the sample contains HBV that may be resistant to anti-HBV drug treatment. While one could conduct additional experimentation to determine whether the presence of a mutation at amino acid position 130 is indicative of the sample containing HBV that may be resistant to anti-HBV drug treatment, the outcome of such research cannot be predicted, and such further research and experimentation are both unpredictable and undue. The instant specification does not provide any guidance to the presence of a mutation at position 130 and the anti-HBV drug lamivudine. In the absence of guidance from the specification, one skill in the art may look to the teachings of the prior art for enablement of a claimed invention. However, the closest prior art references do not provide any guidance to the detection of the presence of a mutation at position 130 as indicative that the sample contains HBV that may be resistant to anti-HBV drug treatment. It is unpredictable as to whether any quantity of experimentation would allow one to practice the claimed invention. Accordingly it would require undue experimentation for a skilled artisan to use the claimed invention.

Response to Arguments

The response traverses the rejection. The response asserts that the amendment to Claim 32 and the cancellation of claim 36 renders the rejection moot. This argument

has been reviewed but is not convincing because the specification nor the art has enabled the method for evaluating whether a sample contains HBV that may be resistant to anti-HBV drug treatment, as set forth in the rejection above. The scope of the claim has been amended and thus, the scope of the rejection has also been amended. Thus for the reasons above and those already of record, the rejection is maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1, 15, 22, 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weinberger et al. (Viral Hepatitis and Liver Disease, pages 138-143, Torino, Edizioni Minerva Medica, 1997) in view of Mbayed et al. (J. Clinical Microbiology, Vol. 36, No. 11, pages 3362-3365, November 1998).

Weinberger et al. (herein referred to as Weinberger) teaches a method of amplification and detection of HBV DNA. Viral DNA was isolated from serum. Primer sequences, which represent highly conserved regions of the s-gene (Table 1) were added to the template DNA. Both the first and second round amplification comprised an initial denaturation step. The amplification was detected and visualized on agarose gels (page 139, col. 1). Sequence analysis of isolates from 14 patients with isolated anti-HBc reactivity are illustrated (page 140). The Table lists the detection of N131T (a mutation at amino acid position 131). Weinberger teaches using primers which span the region comprising the nucleic acid encoding amino acid position 131. Therefore, Weinberger has determined whether the amplified products contain a mutation at amino acid position 131.

Weinberger does not specifically teach using primers of SEQ ID NO: 1 and 2.

However, Mbayed et al. teaches a method for detecting HBV nucleic acid target sequence in a sample, namely serum samples by amplifying the DNA using a nested PCR method to amplify part of the surface gene (page 3362, col. 2)(limitations of Claim 1). The extracted DNA was amplified with primers and then a second round of primer including primers HBS1 and HBS2. The HBS1 primer is 20 nucleotides in length. SEQ ID NO: 1 of the instant application comprises each of the 20 nucleotides of HBS1 with

an additional T nucleotide on the 3' end. HBS2 is immediately downstream of SEQ ID NO: 2 of the instant application, namely four nucleotides downstream at 694-713. As seen in Figure 1, SEQ ID NO: 2 is positions 668-690 of the Figure. These nucleotide positions are conserved among the Gualeguay HBV isolates. The amplification product was sequenced as a means of detection. Mbayed teaches phylogenetic analysis shows "a clear different between the genotype distribution in Buenos Aires, a low-prevalence area, and that found in Gualeguay, Entre Rios, a high prevalence area" (abstract).

Therefore since the claimed oligonucleotides simply represent functional equivalents to the primers taught in the art by Mbayed, the skilled artisan would have been motivated to have designed additional primers which amplified HBV nucleic acids. Given the teachings of Weinberger as to the location of mutations of interest in the HBV genome and Mbayed aligning HBV isolates, the ordinary artisan would have recognized alternative primers which are also within conserved regions of the HBV nucleic acids would be equivalents to the HBS1 and HBS2 primers. The skill in the art at the time the invention was made was very high with respect to designing species or isolate specific primers and for using PCR to amplify regions known to contain mutations. Therefore, the ordinary artisan would have recognized that designing primers which flank a mutation, to further sequence and detect the mutation would have been obvious and routine to the ordinary artisan. Given the specific primers taught by Weinberger for detecting the T131N mutation, the skilled artisan would have been realized that alternative primers would represent functional equivalents. The ordinary artisan would

therefore have the alignment of Mbayed to facilitate designing of nucleic acid primers which would function to amplify nucleic acids flanking the T131N mutation.

Response to Arguments

The response traverses the rejection. The response asserts that the claims are not obvious in view of Weinberger and Mbayed. The response argues that "although SEQ ID NO: 1 shares some sequence identity with that of primer HBS, none of these 2 primer pairs have the same sequence as that of SEQ ID NO: 1 and 2. It is noted that the instant rejection is made under 103 rather than 102. The examiner acknowledges the standard for prima facie case of obviousness as set forth by the response, page 10. This argument has been reviewed but is not convincing because the combination of the references would have suggested all of the claimed limitations, would have provided suggestion to combine the references and there would have been a reasonable expectation of success. The response argues that Weinberger's teaching of numerous regions which are conserved among 30 isolates would not suggest that primer pairs may be modified to have SEQ ID NO: 1 and 2. Further the response argues that Mbayed's teachings of a primer pair that targets a different region of the HBV does not give "a clue as to how Weinberger's primer pairs should be modified to arrive at the claimed method." This argument has been thoroughly reviewed, but is not found persuasive because given the teachings in the art, the ordinary artisan would have targeted known conserved regions for amplifying the region containing the mutation at position 131. Unlike the response's characterization, the primer pair of Mbayed is not to a different region. The forward primer of Mbayed is directed to the exact region

targeted by SEQ ID NO: 1, the forward primer. As noted in the rejection above, the HBS1 primer is 20 nucleotides in length. SEQ ID NO: 1 of the instant application comprises each of the 20 nucleotides of HBS1 with an additional T nucleotide on the 3' end. Further, the reverse primer of Mbayed is directed to a known conserved region, namely positions 694-713. As is clear from Weinberger, region 688-714 is a highly conserved region of the s-gene (Table 1, page 139). Therefore, both SEQ ID NO: 2 and the reverse primer of Mbayed are directed to conserved regions. SEQ ID NO: 2 is four base pairs upstream of the reverse primer taught by Mbayed. This does not constitute a "different region of the HBV." The ordinary artisan would have recognized that designing primers within highly conserved regions would be equivalents. Modifying primers such that the reverse primer is within a known conserved region would have yielded primers with the functionality of amplifying regions between the conserved primers.

In the recent court decision *In Re Deuel* 34 USPQ 2d 1210 (Fed. Cir. 1995), the court determined that the existence of a general method of identifying a specific DNA does not make the specific DNA obvious. Regarding structural or functional homologues, however, the court stated at page 1214:

> "Normally, a *prima facie* case of obviousness is based upon structural similarity, i.e., an established structural relationship between a prior art compound and the claimed compound. Structural relationships may provide the requisite motivation or suggestion to modify known compounds to obtain new compounds. For example, a prior art compound may suggest its homologues because homologues often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties."

The examiner also notes that Deuel teaches at 1215, col. 1, No. 7, "Further, while the general idea of the claimed molecules, their function, and their general chemical nature may have been obvious from Bohlen's teachings, and the knowledge that some gene existed may have been clear, the precise cDNA molecules of claims 5 and 7 would not have been obvious over the Bohlen reference because Bohlen teaches proteins, not the claimed or closely related cDNA molecules". In contrast, in the instant case, the very source of the claimed nucleic acid was provided. The reference even directs the attention to the very region the oligonucleotides are pulled from. Deuel did not find it obvious to probe a library to find full length DNA molecules given a smaller portion of the molecule. The instant case, however, is directed to a known full length molecule and determining smaller molecules which may function as probes and/or primers. Thus, the normal circumstances for a prima facie case should be followed as set out on 1214, col. 2. Weinberger and Mbayed teach the full length region of HBV with specific probes and primers within the nucleic acid.

The response filed December 10, 2003 further argues that a declaration has been filed by Dr. Chong Jin Oon. The response asserts that the declaration filed by Dr. Oon "demonstrates that the primer pair SE QID NO: 1 and 2 are superior to the primer pair MD14/HD03" (page 6 of response filed December 10, 2003). The declaration filed by Dr. Oon has been thoroughly considered, however is not deemed persuasive.

First, the MPEP provides in 716.02(e) a requirement of Comparison With Closest Prior Art. The MPEP states, "An affidavit or declaration under 37 CFR 1.132 must compare the claimed subject matter with the closest prior art to be effective to

rebut a prima facie case of obviousness. In re Burckel, 592 F.2d 1175, 201 USPQ 67 (CCPA 1979). "A comparison of the claimed invention with the disclosure of each cited reference to determine the number of claim limitations in common with each reference, bearing in mind the relative importance of particular limitations, will usually yield the closest single prior art reference." In re Merchant, 575 F.2d 865, 868, 197 USPQ 785, 787 (CCPA 1978) (emphasis in original). Where the comparison is not identical with the reference disclosure, deviations therefrom should be explained, In re Finley, 174 F.2d 130, 81 USPQ 383 (CCPA 1949), and if not explained should be noted and evaluated, and if significant, explanation should be required. In re Armstrong, 280 F.2d 132, 126 USPQ 281 (CCPA 1960) (deviations from example were inconsequential). Applicant does not appear to have compared SEQ ID NO: 1 and 2 to the closest prior art, namely Mbayed (primer HBS1 nad HBS2. The oligonucleotide HBS1 overlaps SEQ ID NO: 1, namely 20/21 nucleotides of SEQ ID NO: 1. The oligonucleotides HBS2 of Mbayed is within the same conserved region as SEQ ID NO: 2 and is 4 base pairs downstream of SEQ ID NO: 2. Applicant has compared SEQ ID NO: 1 and 2 of the instant application to primers directed to nucleotides 418-433 and 734-748. Most importantly, a forward primer directed to positions 418-433 is not the closest prior art to a primer which overlaps 20/21 nucleotides of SE ID NO: 1, namely HBS1 (postions 455-474). The compared primer is also downstream of the claimed primer and does not overlap with the claimed primer in any way. A reverse primer directed to postions 734-748 is not the closes prior art to SEQ ID NO: 2. Mbayed teaches a primer directed to positions 694-713 which is within the same conserved region as taught by Weinberger, namley

conserved positions 688-714. There is no teaching in the art to suggest that 734-748 is a conserved region. Applicant does not appear to have compared SEQ ID NO: 1 and 2 to the closest prior art, namely Mbayed (primers HBS1 and HBS2).

Moreover, MPEP 716.02(d), provides that the unexpected Results must be Commensurate in Scope With Claimed Invention. Applicant has provided an analysis of primers consisting of SEQ ID NO: 1 and 2. The claims are drawn to primers having SEQ ID NO: 1 and 2. Having is open claim language which allows for additional sequences on either end of SEQ ID NO: 1 and 2. As written the claims would encompass a primer which comprises HBS2 and SEQ ID NO: 2. Using this primer, the specificity of the primer to the region would be identical to the results obtained in the art and would not be unobvious. The claims are not drawn to primers consisting of SEQ ID NO: 1-2, thus the results are not commensurate in scope with the nucleic acid sequences.

Thus for the reasons above and those already of record, the rejection is maintained.

9. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Weinberger et al. (Viral Hepatitis and Liver Disease, pages 138-143, Torino, Edizioni Minerva Medica, 1997) in view of Mbayed et al. (J. Clinical Microbiology, Vol. 36, No. 11, pages 3362-3365, November 1998)and further in view of Mason et al. (Hepatology, Vol. 27 (6) 1736-42, June 1998).

Neither Weinberger nor Mbayed specifically teaches specifically teach reverse transcribing mRNA into cDNA prior to analysis.

However, Mason et al. (herein referred to as Mason) teaches hepatic nucleic acid extracts were assessed by PCR for either reverse-transcribed HBV RNA.

Therefore, it would have been prima facie obvious to one of ordinary skill in the art to have modified the methods of Weinberger with the teachings of Mason for reverse transcribing the HBV RNA prior to analysis to obtain DNA. The ordinary artisan would have been motivated to have reverse transcribed the HBV RNA into cDNA for the expected benefit of obtaining DNA which is more stable than RNA. Mason teaches that the reverse transcribed cDNA may be further analyzed by PCR.

Response to Arguments

The response traverses the rejection. The response asserts that Claim 1 has been amended to specify using SEQ ID NO: 1 and 2. This argument has been reviewed but is not convincing because, as explained above, designing primers to known conserved regions would have been obvious in view of the level of skill in the art at the time the invention was made. Mason has been used to teach that a sample may be first reverse-transcribed prior to PCR. Thus for the reasons above and those already of record, the rejection is maintained.

10. Claims 5, 6, 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weinberger et al. (Viral Hepatitis and Liver Disease, pages 138-143, Torino, Edizioni Minerva Medica, 1997) in view of Mbayed et al. (J. Clinical Microbiology, Vol. 36, No. 11, pages 3362-3365, November 1998) and further in view of Dattagupta (EP 0 374 665, June 27, 1990).

Neither Weinberger nor Mbayed specifically teaches the use of a labeled primer or a primer attached to a solid support in combination with a primer in solution.

However, Dattagupta specifically teaches a method for amplifying and detecting specific target nucleic acid sequences in a sample by contacting a first primer and a second primer with nucleic acid where one primer is immobilized and the other primer is labeled (Table 1, embodiments (3) and (6); page 4)(limitations of Claims 6-7). Dattagupta teaches that embodiments (3) and (6) of Table 1 may be assayed for using detection of the label on the support to determine the presence of the test amplified nucleic acid; by hybridization with a specific probe; extent of incorporation of a labeled nucleic acid residue; or a post extension agglutination reaction (page 4, lines 36-43). Dattagupta teaches that in an "immobilizable/labeled system, the biotin would be present on one primer and a label such as fluorescein would be on the second primer, following amplification by thermocycling, the biotin containing product could be immobilized" (page 7, lines 12-16)(limitations of Claim 5). Dattagupta provides that the improvement of the method over the Mullis patent is at least one of the primers is immobilized (page 3, line 34-35). Additionally, Dattagupta teaches that the PCR method is significantly improved by the use of immobilized or immobilizable nucleic acid primers. The final amplified products are already immobilized or specifically immobilizable without significant loss in efficiency of amplification (page 5, lines 9-12).

Therefore, it would have been prima facie obvious to one of ordinary skill in the art to have modified the PCR methods of Weinberger with the teachings of Dattagupta of the improvements of immobilization for detection of PCR products. The ordinary

artisan would have been motivated to have immobilized and labeled the primers of Weinberger for the express benefits taught by Dattagupta. Dattagupta teaches that the "PCR method is significantly improved by the use of immobilized or immobilizable nucleic acid primers. The final amplified products are already immobilized or specifically immobilizable without significant loss in efficiency of amplification." Therefore, the ordinary artisan would have been motivated to have immobilized and labeled the primers in the HBV detection methods for the express benefit of improved detection.

Response to Arguments

The response does not particularly address the rejection containing Dattagupata. Thus for the reasons above and those already of record, the rejection is maintained.

11. Claims 14, 16-21, 24, 26-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Weinberger et al. (Viral Hepatitis and Liver Disease, pages 138-143, Torino, Edizioni Minerva Medica, 1997) in view of Mbayed et al. (J. Clinical Microbiology, Vol. 36, No. 11, pages 3362-3365, November 1998) as applied to Claims 1, 15, 22, 25 above, and further in view of Thanavala et al. (US Pat. 5,531,990, July 1996) and Suzuki et al (International Hepatology Communications, Vol. 4, No. 3, pages 121-125, 1995).

Neither Weinberger nor Mbayed specifically teach mutations as positions 130, 133 or 145.

However, Thanayala teaches that genetic variants of HBV include amino acid substitutions of Gly145Arg in the S protein (col. 13, lines 55-60). Thanalyala also teaches a mutation at position 133.

Moreover, Suzuki teaches mutations in the S region at positions 130, 133 and 145 (see abstract).

Therefore, it would have been prima facie obvious to one of ordinary skill at the time the invention was made to have amplified the region taught by Weinberger in view of Mbayed to contain position 131 to further detect mutations at positions 130, 133 and 145, as taught by Thanayala and Suzuki. The ordinary artisan would have been motivated to have performed a single amplification assay to detect a variety of mutations present in the hypervariable region of the S protein of HBV.

Conclusion

12. No claims allowable over the art.

13. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

A) Birkenmeyer et al. (US Pat. 5,955,598, September 1999) teaches a nucleic acid comprising SEQ ID NO: 2 for detecting the region. See SEQ ID NO: 2 in Table 1.

B) Spies (US Pat. 5,736,334, April 1998) teaches regions to target. Spies teaches targeting position 664-711. SEQ ID NO: 24 comprises SEQ ID NO: 2 of the instant application. Further SEQ ID NO: 17 is directed to a primer which significantly overlaps with the region provided by SEQ ID NO: 2 in the instant application.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jeanine Goldberg whose telephone number is (703) 306-5817. After January 13, 2004, the examiner may be reached at 571-272-0743. The examiner can normally be reached Monday-Friday from 6:00 a.m. to 3:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax number for this Group is (703) 305- 3014.

Any inquiry of a general nature should be directed to the Group receptionist whose telephone number is (703) 308-0196. After January, the receptionist may be reached at (571)272-0507

J. Goldberg

Jeanine Goldberg
Patent Examiner
December 29, 2003

BJ FORMAN, PH.D.
PRIMARY EXAMINER